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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/915,044	07/24/2001	Jeffrey R. Sampson	10980920-1	6010

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EXAMINER
MARSCHEL, ARDIN H

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 12/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M.

Office Action Summary	Application No.	Applicant(s)	
	09/915,044	SAMPSON ET AL.	
	Examiner	Art Unit	
	Ardin Marschel	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) *5-7,10,16-20,22-56,60, & 61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8,9,11-15,21 and 57-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-61* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). [illegible] (4 sheets)
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

RESTRICTION/ELECTION RESPONSE

Applicant's election of Group I, Species A [Methods wherein the semiconductor substrate contains cell(s), which do not contain numerical data storage means], C [Methods wherein an analog-to-digital converter is not present in cell(s) present in the semiconductor substrate], and E [Methods wherein a polymerase is not utilized for incorporating a redox active moiety into a target probe] in the communication, filed 9/26/03, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Consideration of the claims which are readable on all of the elected species in Group I results in claims 1-4, 8, 9, 11-15, 21, and 57-59 being under examination.

TITLE

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is very generic whereas the claims of the elected invention are specific as to electrode activated redox moieties being utilized to produce responses for target detection.

SCOPE OF ENABLEMENT

Claims 1-4, 8, 9, 11-13, and 21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methodology wherein either the redox moiety (claims 14 or 15) is incorporated into a probe or an electronically responsive element lengthens an oligonucleotide probe (claims 57-59), does not

reasonably provide enablement for claim embodiments wherein there is no particular connection between such a moiety or element and a probe molecule which recognizes the desired target molecule. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

The instantly claimed methods are directed to utilizing redox or electronically responsive elements for the detection of a target molecule via probe recognition. Such recognition is, for example, cited in claim 57 wherein oligonucleotide probes bind target molecules for detection. By contrast, instant claim 1 cites the association of a redox moiety to each electrode as well as electrodes comprising a target probe. No

association between the probe and detection redox moiety is present as a limitation. No instant guidance is supplied in the specification regarding what causes the responsive detection signal from the redox moiety other than via probe binding to a target molecule. Therefore, reasonably some type of connection is needed in order that the redox moiety may be utilized for probe/target binding detection. Claim 1, for example, contains no such limitation. Without some type of redox/probe connection for detection the response of the redox moiety to probe/target binding is speculative and unpredictable and therefore lacking in enablement.

Claims 57-59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for oligonucleotide probe detection of target nucleic acid via hybridization, does not reasonably provide enablement for generic binding between an oligonucleotide probe and a target nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in In re Wands, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those

in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a prima facie case are discussed below.

In claims 57-59, the generic binding of an oligonucleotide probe to target nucleic acid is set forth in claim 57; lines 7, 16, and 18; via the limitations; binding, binding, and bound; respectively. It is well known that oligonucleotide recognition of a target nucleic acid occurs via hybridization and not by other generic binding reaction(s). Thus, the citation of the broader limitations directed to binding lacks predictable practice other than via hybridization. Such other generic binding for target nucleic acid recognition by an oligonucleotide probe has not been instantly described and thus lacks enablement.

PRIOR ART

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 8, 9, 11-15, 21, and 57-59 are rejected under 35 U.S.C. 102(e)(1) as being clearly anticipated by De Lumley-woodyear et al. (PreGrant Publication 2002/0081588).

De Lumley-woodyear et al. is a publication directed at electrochemical detection of nucleic acid sequences as summarized in the abstract. In particular Figures 10, 15A, and 15C depict an electrode assembly wherein a redox moiety (polymer) is situated on a electrode to which sample target nucleic acid is hybridized to probe oligonucleotides in what is reasonably interpreted as a detection cell as utilized in the instant claims. The device is described in paragraph 0010 as an array of individual microelectrodes which are individually addressable. A significant instant claim 1 limitation is the activation of the redox moiety via electrode stimulus via addressable stimuli to each electrode. The individual addressable stimuli activation of electrodes, as in instant claim 1, part (b) and (b), subpart (i), is described in paragraphs 0010 and 0011. The redox moiety reaction is further detailed as disclosed in paragraph 0041 wherein the redox moieties are reacted and thus activated for assay usage via "reactive electrophoresis" which deposits and attaches sensor oligonucleotides to the redox polymers on the electrode. This redox activation reads on instant claim 1, part (b), subpart (i). The remainder of instant claim 1 is directed to relatively well known electrode based detection methodology. This electrode based detection methodology is, however, also disclosed in the reference in the sample (with target) depiction in Figure 15C and paragraphs 0042 and 0043 wherein hybridization of the target results in an electrical signal response "if" a target hybridizes to a sensor oligonucleotide as in the last 4 lines of instant claim 1. A general summary of the method of the reference; which also anticipates the overall methodology of the instant claims 1, 2, 12, and 13; is set forth in the reference in paragraphs 0110 – 0111.

The stimulus application via off substrate circuitry in analog values as required for instant claim 4 is set forth in paragraphs 0122 – 0125 in a detailed description of this practice. The individual addressing of such stimuli to each cell is described in the reference in paragraph 0129 as well as the individual addressability in paragraph 0010 which is interpreted as a digital addressability, as in instant claim 3, considering also the large number of sensor cells disclosed in paragraph 0034 ranging from 4 to 10,000.

The reference describes the preparation of redox activated electrodes with probe oligonucleotide prior to sample addition in paragraphs 0040 - 0043, as in instant claims 8 and 14.

Several of the Figures, such as Figure 5, shows the voltammetry detection in the reference as cited in instant claims 11, 21, and 59.

The above pointed to disclosures in the reference include the basic detection methodology of instant 57. The individual detection of a multiplicity of different target nucleic acids as in instant claim 57 is also specifically described in the reference in paragraphs 0013 and 0034. Claim 57 also requires the lengthening of probes which is disclosed in the reference as shown in Figure 15C via redox polymer activation as described above or alternatively via the addition of catalyst to the secondary probe. This catalyst lengthening of the secondary probe is also described in the reference in paragraphs 0043 – 0044.

The sensor oligonucleotides being either DNA or RNA probes, as in instant claim 58, is disclosed in the reference in paragraph 0080.

Another embodiment of the instant claims is directed to the activation of a redox moiety after sample or reaction medium is brought to the electrodes of the invention as required in instant claims 9 and 15. This is disclosed in the reference via the utilization of the secondary probe attachment to the probe complex with a catalyst thereon as summarized in paragraph 0043 – 0044. More detail about this catalyst addition on the secondary probe is set forth in the reference in paragraphs 0090 – 0091. In paragraph 0090 specifically the catalyst is activated in an electrochemical reaction after target hybridization with secondary probe hybridization. In said paragraph 0090, 4th sentence, this electrochemical reaction is described as a electrooxidation or electroreduction. Such oxidation or reduction is reasonably a redox reaction which support the interpretation that such a catalyst is a redox moiety given its redox reactivity.

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703)308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (703)308-4028.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703)305-3524 or to the Technical Center receptionist whose telephone number is (703) 308-0196.

December 12, 2003

ARDIN H. MARSCHEL
PRIMARY EXAMINER